

Report on Microchemical Methods

1193

By C. L. OGG, *Referee* (Eastern Regional Research Laboratory,* Philadelphia 18, Pa.)

Three studies have been conducted during the year. Two are preliminary evaluations of methods for the determination of oxygen and molecular weight and the third is a continuation of the study of the Carius method for the determination of iodine. The collaborators have given us excellent cooperation and the results obtained in all three studies are encouraging.

The results obtained by those collaborators who were asked to repeat the iodine analysis by the method proposed and tested last year were sufficiently improved to warrant recommending the adoption of the method as first action.

The preliminary oxygen study shows a surprising uniformity in the methods used by the collaborators who participated. The results obtained were good both as to accuracy and precision and showed that interference from sulfur was being effectively eliminated. The possibility of obtaining a good official procedure seems excellent.

The study of methods for the molecular weight determination also shows promise of being fruitful. The isothermal distillation procedure, although used by only three collaborators, produced reasonably accurate

results with acceptable precision. A further study of this method seems advisable.

Studies of modifications of the Dumas method are being conducted in the Referee's and other laboratories and it is hoped that a method suitable for testing will be developed.

Since the Referees are aware of no new methods for determining the acetyl group and since the existing methods did not prove satisfactory, studies of this analysis should be discontinued until a more reliable procedure is developed.

It is recommended†—

(1) That the method for iodine used last year and retested this year be adopted as first action.

(2) That the study of methods for molecular weight determination be continued.

(3) That the study of methods for the determination of oxygen be continued.

(4) That studies be continued on the Dumas method for nitrogen.

(5) That the study of methods for the acetyl group be discontinued until a more promising method appears.

† For report of Subcommittee C and action of the Association, see *This Journal*, 41, 27 (1958).

Report on the Micro Determination of Molecular Weights

1194

By C. L. OGG, *Associate Referee* (Eastern Regional Research Laboratory,* Philadelphia 18, Pa.)

The survey conducted last year showed that the molecular weight determination was one of those most in need of collaborative study. Consequently, a preliminary study was conducted this year. Each analyst who participated was asked to use his own

method to determine the molecular weight of two samples, benzoic acid (mol. wt. 122.1) and 3,4-dimethyl-5-sulfanilamido-isoxazole (Gantrisin®, mol. wt. 267.3). The collaborators were asked to perform the analyses in quadruplicate and to furnish certain specific information about the method used. Ten collaborators reported twelve sets of data,

Table 1. Determination of molecular weight by the cryoscopic (Rast) method						
	Coll. 37	Coll. 77	Coll. 23	Coll. 82	Coll. 49	Coll. 2
Benzoic acid (122.1)						
<i>n</i>	6	4	3	3	4	3
\bar{x}	133.0	118.3	137.0	119.3	121.8	122.7
<i>s</i>	4.6	4.0	25	3.2	1.7	3.0
Gantrisin (267.3)						
<i>n</i>	6	4	5	2	—	3
\bar{x}	307	278	268	277	—	278
<i>s</i>	25	6.3	19	—	—	12
Sample wt (mg)	2	0.4–0.7	1.2	1–2	3	8–12
Solvent wt (mg) ^a	15–30	5–10	14	17	30	100
<i>k</i>	40	35.2	36	40	16.49	40.6
Detn exptly	No	—	Yes	No	Yes	Yes
Reference	(1)	(1)	(1)	(1)	(3)	(2)

^a Collaborator 49 used exaltone; all others used camphor.

three by the ebullioscopic method, three by isothermal distillation, and six by the cryoscopic (Rast) procedure.

Results and Recommendation

The results obtained and pertinent information about each procedure used are presented in Tables 1, 2, and 3. The mean (\bar{x}) and standard deviation (*s*) have been calculated for each set of data. The interlaboratory mean ($\bar{\bar{x}}$ or mean of the \bar{x} values) and standard deviation (s_m) also have been calculated. These data are shown in Table 4. The data obtained by the different methods were not compared statistically because of the small number of samples representing the ebullioscopic and isothermal distillation methods.

Inspection of the data shows that the accuracy and precision obtained by the cryoscopic method was lower than those by the

other two methods. The values obtained for Sample 1 (benzoic acid) by the ebullioscopic and isothermal distillation methods were comparable as to intra- and interlaboratory accuracy and precision. For Sample 2 (Gantrisin), however, the intra- and interlaboratory precisions obtained by the isothermal distillation procedure were superior to those of the other two methods.

It appears that the isothermal method should be given a more comprehensive test. The method is based on the principle that when two isothermally isolated solutions are placed with their vapors in contact, distillation takes place until the solutions have the same vapor pressure or are equimolar. The chief objection to this method is the length of time required to obtain equilibrium. Newer procedures, in which the apparatus contains a third well for pure solvent, require three days to make certain that

Table 2. Determination of molecular weight by the ebullioscopic method			
	Coll. 82	Coll. 30	Coll. 29
Benzoic acid (122.1)			
<i>n</i>	4	4	4
\bar{x}	121.3	123.2	123.0
<i>s</i>	1.7	2.2	1.8
Gantrisin (267.3)			
<i>n</i>	4	4	3
\bar{x}	275	248	266
<i>s</i>	15	30	5
Sample wt (mg)	9–10	25–30	20–30
Solvent	acetic acid	acetone	acetone; ethanol
Volume (ml)	5.0	3	10
<i>k</i>	3.07	22.9	35.5; 46.2
Detn exptly	No	No	Yes
Thermometer	Beckman	Water diff.	Hexane diff.
Reference	(9)	(8)	(7)

Table 3. Determination of molecular weight by isothermal distillation			
	Coll. 49	Coll. 57	Coll. 73
Benzoic acid (122.1)			
n	3	4	3
\bar{x}	123.3	122.0	119.3
s	3.2	0.8	3.8
Gantrisin (267.3)			
n	3	3	2
\bar{x}	263.7	267.6	254.0
s	8.6	2.9	—
Sample wt (mg)	10–25	7–15	5
Solvent	acetone	ethyl ether methanol acetone	acetone
Volume (ml)	1	0.5–1.3	1
Standard	acetanilide	azobenzene	benzoic acid
Standard wt (mg)	10	6–22	5
Reference	(4)	(5)	(6)

equilibrium has been established. Points in favor of the method are that a number of solvents can be used, high temperatures are not required, and the apparatus and techniques are relatively simple.

It is recommended* that the study be continued and that more collaborators be encouraged to test the isothermal distillation procedure.

Collaborators

- L. M. White, Western Utilization Research and Development Division
Dorothea A. Ageledis, Hoffmann-La Roche, Inc.
W. A. Struck, The Upjohn Company
Donald Ketchum, Eastman Kodak Co.
G. A. Jones, E. I. duPont de Nemours and Company
L. T. Diuguid and N. C. Johnson, Du-Good Chemical Laboratories
V. A. Aluise, Hercules Powder Company
L. E. Brown, Southern Utilization Research and Development Division
S. A. Schrader, The Dow Chemical Company
C. H. VanEtten, Northern Utilization Research and Development Division

References

- (1) Niederl and Niederl, *Micromethods of Quantitative Organic Analysis*, John Wiley

Table 4. Analysis of interlaboratory data on the determination of molecular weight by three common micromethods

	Cryoscopic (Rast) Method	Ebullioscopic Method	Isothermal Distillation Method
Benzoic Acid (122.1)			
n^a	6	3	3
\bar{x}	125.4	122.5	121.5
s^b	6.9	1.9	2.6
s_m	7.7 (6.3%)	1.0 (0.8%)	2.0 (1.7%)
Gantrisin (267.3)			
n^a	6	3	3
\bar{x}	282.0	263.0	261.8
s^b	16	17	5.8
s_m	17 (6.3%)	14 (5.2%)	7.0 (2.6%)

^a n = number of laboratories.

^b s = average of s values.

- and Sons, Inc., New York, 1942, pp. 217–220.
(2) Aluise, V. A., *Ind. Eng. Chem., Anal. Ed.*, **13**, 365 (1941).
(3) Steyermark, A., *Quantitative Organic Microanalysis*, The Blakiston Co., Philadelphia, 1951, p. 286.
(4) Steyermark, A., *ibid.*, p. 292.
(5) White, L. M., and Morris, R. T., *Anal. Chem.*, **24**, 1063 (1952).
(6) Childs, C. E., *ibid.*, **26**, 1963 (1954).
(7) Menzies, A. W. C., and Wright, S. L., Jr., *J. Am. Chem. Soc.*, **43**, 2314 (1921).
(8) Ketchum, D., *Anal. Chem.*, **19**, 504 (1947).
(9) Niederl and Niederl, *Micromethods of Quantitative Organic Analysis*, 2nd Ed., pp. 212–213.